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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,519	09/22/2003	Andre Stamm	107664.115 US10	5826

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,519	STAMM ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) *1-15,56-80,83 and 84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-55,81 and 82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response to Non-Final Office Action, Applicant's Arguments/Remarks and the Declaration under 37 C.F.R. §1.132, all filed 3/5/07 is acknowledged.

Claims 1-84 are pending in this action. Claims 1-15, 56-80, 83 & 84 have previously been withdrawn (due to non-elected subject matter). No amendments to the claims have been made herein. Claims 16-55, 81 & 82 remain rejected.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 16-25, 32-34, 36-45, 52-54, 81 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyer (US Pat. No. 4,800,079).

The instant invention is drawn to a fenofibrate composition comprising granulates, wherein the granulates comprise micronized fenofibrate, inert carrier particles, at least one hydrophilic polymer and at least one disintegrant, wherein the weight ratio of micronized fenofibrate to hydrophilic polymer is between 1:10 and 4:1.

Boyer ('079) teaches a fenofibrate composition comprising granules, wherein each granule comprises an inert core constituted with hydrosoluble carrier particles (lactose, sucrose, glucose), a hydrophilic polymer (polyvinylpyrrolidone) and a fenofibrate layer and a protective layer wherein the fenofibrate is in the form of crystalline microparticles having a particle size of

not greater than 30 microns and preferably less than 10 microns (see abstract and reference columns 2-4). Starch (disintegrant) can also be included in the composition (Claims 3 & 7).

Boyer teaches fenofibrate granules wherein the inert matrix is composed by a binder selected from the group comprising: *methacrylic polymers, polyvinylpyrrolidone, mixtures thereof; cellulose derivatives; and polyethylene glycols* (claim 2). The inert core is constituted by a substance selected from the group comprising: *glucose, sucrose, lactose and their equivalents, starch and mixtures thereof* (claim 3). The fenofibrate composition includes a protective coating layer, representing about 1% by weight of each granule and is formed of a substance selected from the group comprising: *methacrylic polymers, polyvinylpyrrolidone, mixtures thereof; cellulose derivatives; and polyethylene glycols* (claim 4). The amount of binder is such that the quantity of fenofibrate liberated in one hour in an aqueous liquid is not less than 65% (claim 5). The dimensions of the microparticles are *less than 10 microns* (claim 6).

Boyer teaches that the granules obtained are put into capsules with a dose of 250 mg of fenofibrate per capsule. Boyer teaches that the fenofibrate layer is similar to that of a sponge, with the pores containing microparticles of fenofibrate. A binder, methacrylate or polyvinylpyyrolidone, which is soluble in aqueous medium, constitutes the sponge. Once the binder has dissolved, the microparticles of fenofibrate are released. The amount of binder is determined so that at least 65% of the fenofibrate is released in one hour in a water-based liquid medium (col. 3, lines 10-45).

Boyer teaches that the inert grains for forming the inert cores can have a diameter adjusted from 0.3 mm (or 300 microns) to 0.6 mm (or 600 microns) (col. 2, lines 38-51).

In the Example at col. 3, fenofibrate is provided in amounts of 400 kg, inert grains (sugar and/or starch) are provided in amounts of 110 kg and polyvinylpyrrolidone and/or methacrylate are provided in amounts of 20 kg. Thus, the weight ratio of fenofibrate: polyvinylpyrrolidone and/or methacrylate is 20:1.

While Boyer does not explicitly teach the instantly claimed weight ratio of fenofibrate to hydrophilic polymer, nor the instant amounts of fenofibrate, carrier and hydrophilic polymer as claimed in claims 32-33 & 52-53, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this instance, Applicants have not demonstrated any superior or unexpected results, which accrue from the claimed weight ratios or amounts. The prior art recognizes and teaches similar formulations comprising similar ingredients, intended to treat the same problems as that desired by Applicants. No patentable distinction has been observed, which accrues from the instant amounts claimed since effective results are obtained using the compositions of Boyer.

With regards to instant claims 81 and 82, the granules of Boyer comprised of fenofibrate would be in non-reagglomerated form.

Given the explicit teachings of Boyer, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 16-55, 81 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtet *et al.* (US Pat. No. 4,895,726).

The instant invention is drawn to a fenofibrate composition comprising granulates, wherein the granulates comprise micronized fenofibrate, inert carrier particles, at least one hydrophilic polymer and at least one disintegrant, wherein the weight ratio of micronized fenofibrate to hydrophilic polymer is between 1:10 and 4:1.

Curtet *et al.* ('726) teach a fenofibrate composition comprising fenofibrate granules in combination with a solid surfactant, wherein the fenofibrate and solid surfactant have been co-micronized; a hydrosoluble carrier and a hydrophilic polymer, wherein the fenofibrate/solid surfactant mixture granules have a mean particle size of less than 15 microns (see column 1, line 1 – col. 2, line 25); examples and claims.

Curtet *et al.* teach polyvinylpyrrolidone as the hydrophilic polymer employed. The hydrosoluble carrier taught is lactose (col. 2, lines 1-12). The preferred solid surfactant is sodium lauryl-sulfate in a recommended amount of between 0.5% and 7% (col. 1, lines 52-58). Excipients, such as magnesium stearate (lubricant) and starch (distintegrant) may also be added (col. 2, lines 1-4).

Curtet *et al.* teach a micronized fenofibrate composition containing a micronized mixture of particles of fenofibrate and a solid surfactant and method for preparing the fenofibrate composition comprising (i) intimately mixing and then co-micronizing the fenofibrate and the solid surfactant, (ii) adding lactose and starch to the mixture obtained, (iii) converting the whole to granules in the presence of water, (iv) drying the granules until they contain no more than 1%

of water, (v) grading the granules, (vi) adding polyvinylpyrrolidone and magnesium stearate to the graded granules and (vii) filling gelatin capsules with the mixture obtained in stage (vi). The mean particle size of the micronized mixture obtained is less than 15 microns (μm) (column 2, lines 5-20).

Curtet *et al.* teach effective amounts of fenofibrate and a hydrophilic polymer-polyvinylpyrrolidone, wherein the fenofibrate is present in an amount of 200 mg per therapeutic unit (col. 1, lines 50-51) and the polyvinylpyrrolidone is contained in an amount of 7 mg (col. 3, lines 21-32).

While Curtet *et al.* do not explicitly teach the instantly claimed weight ratio of fenofibrate:hydrophilic polymer; surfactant:hydrophilic polymer, nor the instant amounts of fenofibrate and carrier as claimed in claims 32-33 & 52-53, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this instance, Applicants have not demonstrated any superior or unexpected results, which accrue from the claimed weight ratios or amounts. The prior art vividly recognizes and teaches similar formulations comprising similar ingredients (fenofibrate, polymer, inert particles, etc.) that are used in the same field of endeavor to effectively treat the same problems (*i.e.*, hypercholesterolemia) as that desired by Applicants. No patentable distinction has been observed, which accrues from the instant amounts claimed since effective results are obtained using the compositions of Curtet *et al.*

Hence, given the explicit teachings of the art delineated above, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 03/05/07 have been fully considered but they are not persuasive.

Rejection under 35 U.S.C. 103(a) over Boyer (US 4,800,079):

Applicant argued, "Applicants respectfully submit that Boyer does disclose or suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1 as recited in independent claims 16 and 36. Boyer discloses a composition containing micronized fenofibrate, a polymer such as polyvinylpyrrolidone (PVP), and possibly starch. The sole example that is provided in BoyerI comprises 400 kg of fenofibrate and 20 kg of PVP and/or methacrylate. As correctly pointed out by the U.S. Patent Office (PTO), Boyer's ratio of fenofibrate to polymer is 20:1. Boyer does not provide any motivation or suggestion to drastically reduce the weight ratio of fenofibrate to PVP of 20:1 to be any where near the claimed range of fenofibrate to polymer of between 1:10 and 4:1. The weight ratio in Boyer is significantly different than the claimed weight ratio and there is no motivation or suggestion to arrive at the claimed weight ratio of between 1:10 and 4:1. The ratio of fenofibrate to polymer in Boyer has more than 5 times fenofibrate to PVP than the claimed ratio of fenofibrate to polymer. One skilled in the art could not use routine experimentation to arrive at the claimed ratio because it would require one to drastically reduce Boyer's ratio to be 5 times less than stated to arrive at the claimed invention. Routine variation or experimentation would revolve around Boyer's ratio of 20:1, and not the claimed ratio that is 5 times smaller. In view of the significant difference in the ratios, the claimed ratio is not encompassed by Boyer and is not merely an optimization of the ratio described by Boyer. Although the criticality of the claimed range is not required because the PTO has not established a prima facie case of obviousness, Applicants have provided data showing the criticality of the claimed range, as discussed below. The dissolution medium and conditions in the present claims are a rotating blade method at 75 rpm, where the dissolution medium is water with 2% polysorbate 80 or water with 0.025 M sodium lauryl sulfate. In contrast, Boyer uses 35 ml of a medium having a pH of 1.5, and a stirring speed of 30 rpm at 37°C. Having a different pH and rotating speed will influence dissolution. Accordingly, it is necessary to compare the composition described in Boyer and the claimed composition using the same method. In support of the fact that the invention provides unexpectedly superior results over Boyer, Applicants refer to the Declaration under 37 C.F.R. § 1.132 by Philippe Reginault (hereafter the Reginault Declaration) attached hereto and submitted in the related case of US Application No. 10/288,425. The Reginault Declaration provides a direct comparison between Boyer and the claimed invention. It is known in the art that the composition described by Boyer is represented by Lipanthyl® 250. See Reginault Declaration at ¶ 7. The composition recited in the claims is represented in the specification at Example 2 and by Lipanthyl® Supra. See Reginault Declaration at ¶. A comparison of the dissolution profile of Boyer (i.e., Lipanthyl® 250) and the claimed invention (i.e., Lipanthyl® Supra) is shown in Tables 1 and 2 and Figures 1 and 2 in the Reginault Declaration at ¶ 11. As shown in the Reginault Declaration at ¶ 13 and the specification at Example 2, the presently claimed invention has an unexpectedly superior dissolution profile when compared to Boyer. Accordingly, one skilled in the art would not arrive at the presently claimed invention based on the teachings in Boyer."

Applicant's arguments have been thoroughly considered, but were not persuasive. Admittedly, while Boyer do not teach the claimed fenofibrate to polymer ratio claimed of between 1:10 and 4:1, it remains the position of the Examiner that such claimed ratios are attainable by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results. The claimed ratios, which, albeit are reduced weight ratios in comparison with Boyer, who teaches a fenofibrate to polymer ratio of 20:1, nonetheless, do not render a *patentable* distinction over the explicit reference teachings. Boyer vividly teaches a similar composition as claimed, comprising the same components (i.e., fenofibrate, polymer, distintegrant, etc.) formulated for the same field of endeavor and purpose as that of the Applicants. The argument that "the sole example in Boyer comprises 400 kg of fenofibrate and 20 kg of PVP and/or methacrylate; (20:1 ratio) was not persuasive since the teachings of the prior art are not limited to the examples demonstrated therein. The reference as a whole is being considered for what it explicitly teaches. Applicant's argument that "the instant invention provides an unexpectedly superior profile when compared to Boyer" was not persuasive since dissolution profiles are not what are being claimed herein. In any event, Boyer meets the requirements of incorporating micronized fenofibrate, hydrophilic polymer and disintegrant components, the only deficiency being the claimed weight ratios, which as noted above, is a routinely optimized parameter that is attainable within the art.

Rejection under 35 U.S.C. 103(a) over Curtet (US 4,895,726):

Applicant argued, "Applicants respectfully submit that Curtet does disclose or suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1 as recited in independent claims 16 and 36. Curtet provides working examples comprising 200 grams fenofibrate and 7 grams cross-linked polyvinylpyrrolidone, such that the weight ratio of fenofibrate to cross-linked polyvinylpyrrolidone is 29:1. Curtet does not provide any motivation or suggestion to drastically reduce the weight ratio of fenofibrate to polyvinylpyrrolidone (PVP) of 29:1 to the claimed

range of fenofibrate to polymer of between 1:10 and 4:1. The weight ratio in Curtet is significantly different than the claimed weight ratio and there is no motivation or suggestion in any of the references to arrive at the claimed weight ratio of between 1:10 and 4:1. The ratio of fenofibrate to polymer in Curtet has greater than 7 times more fenofibrate to PVP than the claimed ratio of fenofibrate to polymer. There is simply no motivation in Curtet to drastically reduce the ratio used in Curtet to arrive at the claimed invention.
Curtet corresponds to EP-A-0330532 which is discussed in the specification at page 2, lines 1-20 and Examples 2-4. Curtet corresponds to Lipanthyl® 200M in Figures 1 and 2 in the present application. The dissolution medium and conditions in the present claims are a rotating blade method at 75 rpm, where the dissolution medium is water with 2% polysorbate 80 or water with 0.025 M sodium lauryl sulfate. In contrast, Curtet uses a rotating vane or continuous flow cell where the dissolution medium is water with 0.1 M sodium lauryl sulfate. The dissolution medium of Curtet comprises much more sodium lauryl sulfate (i.e., surfactant) than the dissolution medium of the claimed invention. Having more surfactant will necessarily enhance dissolution. Accordingly, it is necessary to compare the composition described in Curtet and the claimed composition using the same method. This was done in the present application.
Applicants have shown in Example 2 and Figure 1 of the present application that the claimed invention has an unexpectedly superior dissolution profile compared to Lipanthyl® 200M as described by Curtet. The claimed invention achieves 75% dissolution in 30 minutes, and Inventive Example 2 achieves 95.9% dissolution in 30 minutes. The data in the Laboratory Notebook submitted to the PTO shows that it takes 60 minutes for Curtet's Lipanthyl® 200M to achieve a dissolution of 78%. Blouquin Declaration at ¶ 15. In other words, it takes almost twice as long for Curtet's Lipanthyl® 200M to achieve a dissolution that the claimed fenofibrate composition can achieve in 30 minutes. Blouquin Declaration at ¶ 15. In view of these results, it is Ms. Blouquin's opinion that the claimed invention is superior to Curtet's Lipanthyl® 200M. Blouquin Declaration at ¶ 15. Curtet fails to provide any motivation for one skilled in the art to modify the fenofibrate to polymer ratio. Curtet is solely concerned with co-micronization, and provides no guidance as to the relevancy of the amount of fenofibrate or polymer. Hence, Curtet does not provide motivation to modify the ratio of fenofibrate to polymer to arrive at the claimed ratio."

Applicant's arguments have been fully considered, but were not persuasive. Examiner agrees that Curtet do not teach the claimed fenofibrate to polymer ratio claimed of between 1:10 and 4:1. However, it is the position of the Examiner that Applicants have not yet established a patentable distinction, which accrues from the claimed weight ratios of fenofibrate to polymer. Applicant argues that the "instant invention provides for an unexpectedly superior dissolution profile compared to Lipanthyl® 200M as described by Curtet", yet the dissolution profile comparison presented by Applicant does not deter the teachings of Curtet, since Curtet essentially teaches a composition that is very similar to the one being claimed by Applicant, the only distinction being the claimed ratios. Moreover, Applicants' argument establishing superior dissolution profiles is not what is being claimed. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van*

Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In this instance, there is no criticality observed in the instant weight ratios, since the prior art clearly discloses and suggests effective fenofibrate formulations, comprising the same ingredients, for the same intended purpose and same field of endeavor to solve the same problem as that desired by Applicants.

The Declaration under 37 C.F.R. §1.132 filed 3/5/07 has been considered but was not persuasive. The Declaration provides a comparison of the dissolution profiles of Lipanthyl®250 (Boyer) and Lipanthyl® Supra (instant invention), however, the Declaration does not establish the scope of claims being presented. For instance, the instant claims are silent with respect to any desired dissolution profiles of fenofibrate. The independent claims merely recite a weight ratio of between 1:10 and 4:1 of fenofibrate to hydrophilic polymer, but do not recite the dissolution profiles presented by Applicant in the §1.132 Declaration. Thus, Applicant's arguments do not establish the scope of claims being presented.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Primary Examiner

Art Unit 1615

May 18, 2007

HUMERA N SHEIKH
PRIMARY EXAMINER
TC-1600

hns